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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/151,409	09/10/98	DALE J	481112.410

EXAMINER	
LEE, L	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)

1- File Copy

Office Action Summary	Application No. 09/151,409	Applicant(s) Dale
	Examiner Li Lee	Group Art Unit 1645

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-11 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-11 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☒ The drawing(s) filed on 9-10-98 is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Drawings

1. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsperson under 37 C.R.F. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims 1-11 are indefinite for using the phrase "a peptide C terminal to the immunogenic polypeptide". It is not clear what is "a peptide", such might indicate that "a peptide" is different separate peptide from the immunogenic polypeptide, or alternatively might be intended to indicate that the C-terminal of the immunogenic polypeptide. Claims 1-11 are further indefinite for reciting the limitation "the C-terminal peptide" in (b). There is insufficient antecedent basis for this limitation in the claim.

Claims 2-4 and 6-8 are indefinite as it not clear what limitation is implied by the recitation of "serotype". Without specific serologic antigen-antibody type, the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 5, and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Dale (J Immunol.. 151(4): 2188-2194, 1993) or Dale (Vaccine 14 (10):944-8, 1996 (Jul)).

Claims 1, 5, and 9-11 are drawn to an immunogenic fusion polypeptide/a vaccinating agent has at least two immunogenic polypeptide at least 10 amino acids in length from a group A streptococci. The C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci. A method for vaccinating against group A streptococci infection by administering the vaccinating agent. The vaccinating agent is further comprising a Freund's adjuvant.

Dale (J Immunol.151(4): 2188-2194, 1993) or Dale (Vaccine 14 (10):944-8, 1996 (Jul)) teaches a recombinant multivalent group A streptococcal vaccine which has at least two

immunogenic fusion polypeptide more than 10 amino acids in length (see Abstract and Materials and Methods). When the multivalent peptides are ligated in tandem (Dale (JI)) or covalently linked to KLH (Dale (Vaccine)) it generates a non-immunogenic C-terminus for the immunogenic polypeptide. These recombinant proteins are immunogenic and elicit protective immune responses against group A streptococci in the test hosts which indicate that the C-terminal immunogenic polypeptide protects the immunogenicity of the immunogenic polypeptide portion and the C-terminal immunogenic polypeptide is non-immunogenic for immune response against group A streptococci. Dale (JI)/Dale (Vaccine) also teaches that the recombinant multivalent group A streptococcal vaccine is used with a Freund's adjuvant. Thus Dale's teachings meet the limitations of the claims.

6. Claims 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Dale (J Exp Med 163:1191-1202, 1986)

Claims 5 and 6 are drawn to a vaccinating agent which has at least two immunogenic polypeptides at least 10 amino acids in length from a serotype 5 group A streptococci. The C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci.

Dale (J Exp Med 163:1191-1202, 1986) teaches a multivalent group A streptococcal vaccine which has at least two immunogenic polypeptides more than 10 amino acids in length (see

Abstract and Materials and Methods) from a serotype 5 group A streptococci. When the multivalent peptides are covalently linked to KLH it generates a non-immunogenic C-terminus for the immunogenic polypeptide. The multivalent vaccine is immunogenic and elicits protective immune responses against group A streptococci in the test hosts which indicate that the C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic polypeptide portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci thus meeting the limitations of the claims.

7. Claims 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Beachey (J Immunol. 136(3):2287-92, 1986).

Claims 5 and 7 are drawn to a vaccinating agent which has at least two immunogenic polypeptides at least 10 amino acids in length from a serotype 6 group A streptococci. The C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci.

Beachey (J Immunol. 136(3):2287-92, 1986) teaches a multivalent group A streptococcal vaccine which has at least two immunogenic polypeptides more than 10 amino acids in length (see Abstract and Materials and Methods) from a serotype 6 group A streptococci. When the multivalent peptides are conjugated to tetanus toxoid it generates a non-immunogenic C-terminus for the immunogenic polypeptide. The multivalent vaccine is immunogenic and elicits protective

immune responses against group A streptococci in the test hosts which indicate that the C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic polypeptide portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci thus meeting the limitations of the claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dale (J Exp Med 163:1191-1202, 1986) and Dale ((J Immunol.. 151(4): 2188-2194, 1993).

Claims 1 and 2 are drawn to an immunogenic fusion polypeptide which has at least two immunogenic polypeptides at least 10 amino acids in length from a serotype 5 group A streptococci. The C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci.

Dale (J Exp Med 163:1191-1202, 1986) teaches a immunogenic polypeptide of group A streptococcal which has at least two immunogenic polypeptides more than 10 amino acids in length (see Abstract and Materials and Methods) from a serotype 5 group A streptococci. When the multivalent peptides are covalently linked to KLH it generates a non-immunogenic C-terminus

for the immunogenic polypeptide. The multivalent vaccine is immunogenic and elicits protective immune responses against group A streptococci in the test hosts which indicate that the C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic polypeptide portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci.

Dale (J Exp Med 163:1191-1202, 1986) does not teach making immunogenic fusion polypeptides.

Dale (J Immunol.. 151(4): 2188-2194, 1993) teaches a recombinant multivalent group A streptococcal vaccine which has at least two immunogenic fusion polypeptides more than 10 amino acids in length (see Abstract and Materials and Methods). When the multivalent peptides are ligated in tandem (Dale (JI)) or covalently against group A streptococci in the test hosts which indicate that the C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic polypeptide portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci. linked to KLH (Dale (Vaccine)) it generates a non-immunogenic C-terminus for the immunogenic polypeptide. These recombinant proteins are immunogenic and elicit protective immune responses.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to generate immunogenic fusion polypeptide from serotype 5 group A streptococci using the method of Dale (J Immunol.. 151(4): 2188-2194, 1993) in place of the immunogenic chemical synthetic polypeptide of Dale (J Exp Med 163:1191-1202, 1986) to

attain the known and disclosed advantage of a fusion protein which includes high accuracy peptide sequence, reproducibility, and provision for an unlimited supply of reagent.

10. Claima 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beachey (J Immunol. 136(3):2287-92, 1986) and Dale ((J Immunol.. 151(4): 2188-2194, 1993).

Claims 1 and 3 are drawn to an immunogenic fusion polypeptide which has at least two immunogenic polypeptides at least 10 amino acids in length from a serotype 6 group A streptococci. The C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci.

Beachey (J Immunol. 136(3):2287-92, 1986) teaches a immunogenic polypeptide of group A streptococcal which has at least two immunogenic polypeptides more than 10 amino acids in length (see Abstract and Materials and Methods) from a serotype 6 group A streptococci. When the multivalent peptides are conjugated to tetanus toxoid it generates a non-immunogenic C-terminus for the immunogenic polypeptide. The multivalent vaccine is immunogenic and elicits protective immune responses against group A streptococci in the test hosts which indicate that the C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic polypeptide portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci.

Beachey (J Immunol. 136(3):2287-92, 1986) does not teach making immunogenic fusion polypeptides.

Dale (J Immunol.151(4): 2188-2194, 1993) teaches a recombinant multivalent group A streptococcal vaccine which has at least two immunogenic fusion polypeptides more than 10 amino acids in length (see Abstract and Materials and Methods). When the multivalent peptides are ligated in tandem it generates a non-immunogenic C-terminus for the immunogenic polypeptide. These recombinant proteins are immunogenic and elicit protective immune responses against group A streptococci in the test hosts which indicate that the C-terminus of immunogenic fusion polypeptide protects the immunogenicity of the immunogenic polypeptide portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci..

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to generate immunogenic fusion polypeptide from serotype 6 group A streptococci using the method of Dale (J Immunol.. 151(4): 2188-2194, 1993) in place of the immunogenic chemical synthetic polypeptide of Beachey (J Immunol. 136(3):2287-92, 1986) to attain the known and disclosed advantage of a fusion protein which includes high accuracy, reproducibility, and provision for an unlimited supply of reagent.

11. Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dale (J Immunol.. 151(4): 2188-2194, 1993) and Beall (J Clin Microbiol 34 (4):953-8, 1996).

Claims 1 and 4 are drawn to an immunogenic fusion polypeptide which has at least two immunogenic polypeptides at least 10 amino acids in length from a serotype selected from the

group 1, 1.1, 2-4, 11-14, 18-19, 22, 28, 30, 48, 52, and 56 of group A streptococci. The C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci.

Dale (J Immunol. 151(4): 2188-2194, 1993) teaches a recombinant multivalent group A streptococcal vaccine which has at least two immunogenic fusion polypeptides more than 10 amino acids in length (see Abstract and Materials and Methods). When the multivalent peptides are ligated in tandem it generates a non-immunogenic C-terminus for the immunogenic polypeptide. These recombinant proteins are immunogenic and elicit protective immune responses against group A streptococci in the test hosts which indicate that the C-terminus of immunogenic polypeptide protects the immunogenicity of the immunogenic polypeptide portion and the C-terminus of immunogenic polypeptide is non-immunogenic for immune response against group A streptococci.

Dale (J Immunol. 151(4): 2188-2194, 1993) does not teach making an immunogenic fusion polypeptide from a serotype selected from the group 1, 1.1, 2-4, 11-14, 18-19, 22, 28, 30, 48, 52, and 56 of group A streptococci.

Beall (J Clin Microbiol 34 (4):953-8, 1996) discloses serologic M types M1-M80 including the group 1, 1.1, 2-4, 11-14, 18-19, 22, 28, 30, 48, 52, and 56 of group A streptococci.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the serologic group 1, 1.1, 2-4, 11-14, 18-19, 22,

28, 30, 48, 52, and 56 of group A streptococci of Beall (J Clin Microbiol 34 (4):953-8, 1996) for serotype 5 of Dale (J Immunol.. 151(4): 2188-2194, 1993) to generate vaccines against medical impotent serotypes 1, 1.1, 2-4, 11-14, 18-19, 22, 28, 30, 48, 52, and 56 of group A streptococci by using known and disclosed immunoprotactive M proteins in these groups.

Citation of Pertinant Art

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Wittner (Infection and Immunity 15(1) :104-108, 1977) teaches use alum as adjuvant for M protein vaccination. Beachey et al (US Patent 4,919,930) teaches synthetic peptide segments of protein Pep M5.

Status of Claims

13. No claims are allowed. All claims stand rejected.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Lee, M.D., Ph.D. whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Li Lee, M.D., Ph.D.
May 24, 1999

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